

=> file registry
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 08:02:03 ON 19 FEB 2008
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STRUCTURE FILE UPDATES: 18 FEB 2008 HIGHEST RN 1004360-55-7
DICTIONARY FILE UPDATES: 18 FEB 2008 HIGHEST RN 1004360-55-7

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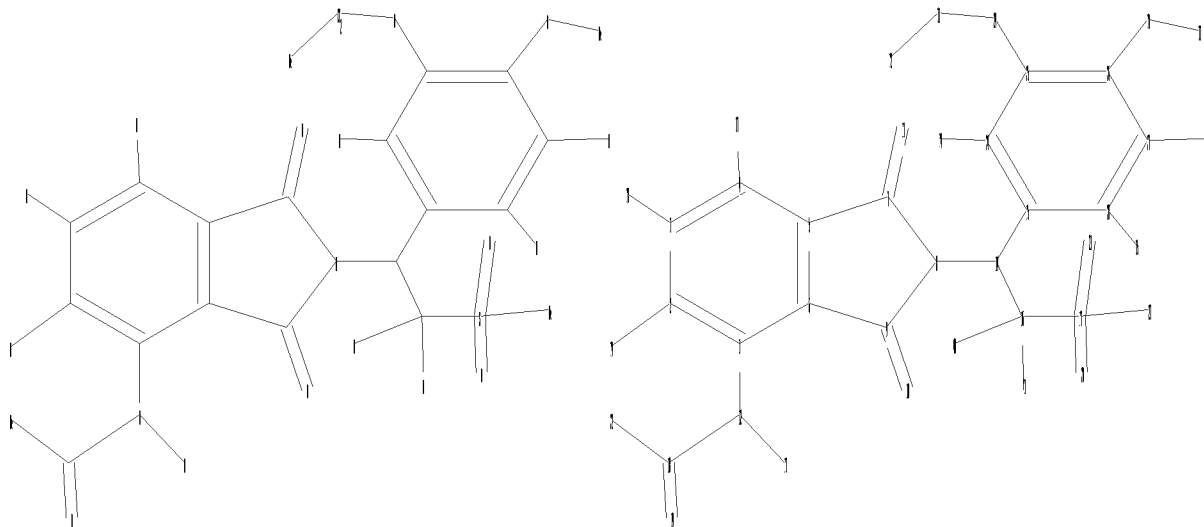
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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Uploading C:\Program Files\Stnexp\Queries\10693722claim1.str



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10 11 12 13 14 16 17 18 19 20 21 22 23 29 30 31 32 33 34 35 36
37 38 39 40 41
ring nodes :
1 2 3 4 5 6 7 8 9 15 24 25 26 27 28
chain bonds :
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30-33 31-32

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ring bonds :
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27-28
exact/norm bonds :
1-12 5-7 6-9 7-8 7-11 8-9 8-14 9-10 12-18 16-17 17-20 17-21 18-19 25-29
26-30
exact bonds :
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normalized bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:CLASS
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L1 STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

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100.0% PROCESSED          5 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01

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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
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PROJECTED ITERATIONS:   5 TO      234
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L3 3 SEA FAM FUL L1

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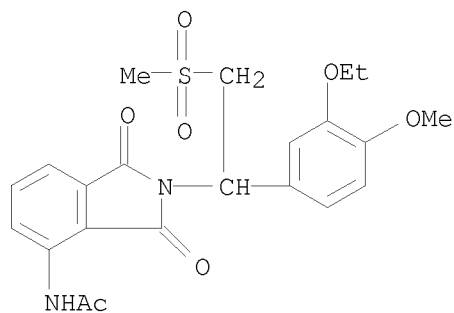
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L3 3 ANSWERS  REGISTRY  COPYRIGHT 2008 ACS on STN
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MF  C22 H24 N2 O7 S

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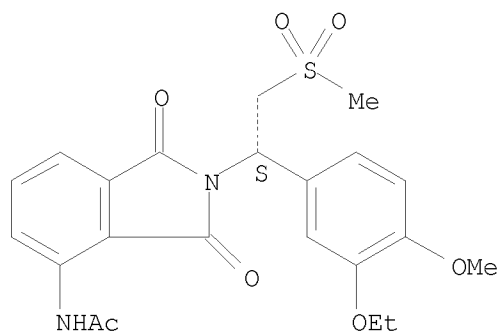


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L3 3 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
 IN Acetamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(
 (methylsulfonyl)ethyl]-2,3-dihydro-1,3-dioxo-1H-indol-4-yl]-
 MF C22 H24 N2 O7 S

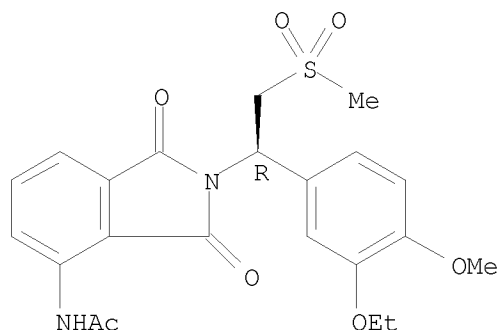
Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 3 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
 IN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-2-(
 (methylsulfonyl)ethyl]-2,3-dihydro-1,3-dioxo-1H-indol-4-yl]-
 MF C22 H24 N2 O7 S

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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0 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

70.11

70.32

FILE 'CAPLUS' ENTERED AT 08:02:39 ON 19 FEB 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 19 Feb 2008 VOL 148 ISS 8

FILE LAST UPDATED: 18 Feb 2008 (20080218/ED)

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=> s 13

L4 19 L3

=> s 14 and (PY<2003 or AY<2003 or PRY<2003)

22928631 PY<2003
4476249 AY<2003
3951450 PRY<2003

L5 10 L4 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> d 15 1-10 ti abs bib

L5 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration and Methods of using thereof

AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Thus, patients with macular degeneration received conventional therapy with verteporfin and (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminisoindoline 1,3-dione in an amount of about 20 mg/day as an adjuvant for 20 wk. The neovascular cascade was sufficiently hindered in those patients to indefinitely prolong the effects of the photodynamic therapy.

AN 2007:998162 CAPLUS <<LOGINID::20080219>>

DN 147:330440

TI Compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration and Methods of using thereof

IN Zeldis, Jerome B.

PA USA

SO U.S. Pat. Appl. Publ., 30pp., Cont.-in-part of U.S. Ser. No. 699,110.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

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| PRAI | US 2003-699110 | A2 | 20031030 | | |
| | WO 2004-US13253 | W | 20040428 | | |
| | US 2002-422900P | P | 20021031 | <-- | |
| OS | MARPAT 147:330440 | | | | |

L5 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Methods of the treatment or prevention of exercise-induced asthma using (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminisoindoline-1,3-dione

AB Methods of treating, managing or preventing exercise-induced asthma are disclosed. Specific methods encompass the administration of

(+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione alone or in combination with a second active agent. Pharmaceutical compns. and single unit dosage forms are also disclosed.

AN 2006:823362 CAPLUS <<LOGINID::20080219>>

DN 145:224862

TI Methods of the treatment or prevention of exercise-induced asthma using (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione

IN Muller, George W.; Schafer, Peter H.; Rohane, Patricia E. W.

PA Celgene Corporation, USA

SO U.S. Pat. Appl. Publ., 32pp., Cont.-in-part of U.S. Ser. No. 106,142.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
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| | US 6962940 | B2 | 20051108 | | | |
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| | US 2003-438450P | P | 20030107 | | | |
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| | CN 2003-811093 | A3 | 20030320 | | | |
| | US 2005-170308 | A3 | 20050628 | | | |

RE.CNT 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Methods of the treatment of psoriatic arthritis using (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione

AB Methods of treating, managing or preventing psoriatic arthritis are disclosed. Specific methods encompass the administration of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione alone or in combination with a second active agent. Pharmaceutical compns. and single unit dosage forms are also disclosed.

AN 2006:821184 CAPLUS <<LOGINID::20080219>>

DN 145:224861

TI Methods of the treatment of psoriatic arthritis using (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione

IN Muller, George W.; Schafer, Peter H.; Rohane, Patricia E. W.

PA Celgene Corporation, USA

SO U.S. Pat. Appl. Publ., 19pp., Cont.-in-part of U.S. Ser. No. 106,142.
CODEN: USXXCO

DT Patent

LA English

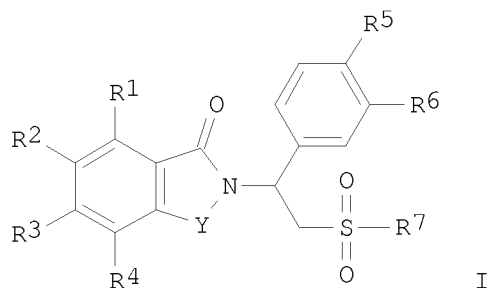
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| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
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| | US 2008027123 | A1 | 20080131 | US 2007-824523 | 20070629 <-- |
| PRAI | US 2002-366515P | P | 20020320 | <-- | |
| | US 2003-438450P | P | 20030107 | | |
| | US 2003-392195 | A3 | 20030319 | | |
| | US 2005-106142 | A2 | 20050413 | | |
| | CN 2003-811093 | A3 | 20030320 | | |
| | US 2005-170308 | A3 | 20050628 | | |

RE.CNT 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of substituted phenethyl sulfones and methods of reducing
 TNF α levels
 GI



AB The title compds. I [Y = CO, CH₂, SO₂, CH₂C(O); R₁-R₄ = H, halo, alkyl, alkoxy, etc.; R₅, R₆ = H, alkyl, alkoxy, CN, etc.; R₇ = OH, alkyl, Ph, etc.], useful for reducing TNF α levels and treating inflammatory and autoimmune diseases, were prepared and formulated. E.g., a 2-step synthesis of 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]isoindolin-1-one, starting from di-Me sulfone and 3-ethoxy-4-methoxybenzaldehyde, was given.

AN 2006:425851 CAPLUS <<LOGINID::20080219>>
 DN 147:189068

TI Preparation of substituted phenethyl sulfones and methods of reducing
 TNF α levels

IN Man, Hon-Wah; Muller, George W.

PA Celgene Corporation, USA

SO Aust. Pat. Appl., 53 pp.

CODEN: AUXXCM

DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI | AU 2006200033 | A1 | 20060202 | AU 2006-200033 | 20060106 |
| | AU 2003203681 | A1 | 20030703 | AU 2003-203681 | 20030409 <-- |
| PRAI | AU 2003-203681 | A3 | 20030409 | | |
| | AU 2000-14472 | A3 | 19991019 | <-- | |
| | WO 1999-US24376 | W | 19991019 | <-- | |

L5 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration
 AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with macular degeneration were treated by photodynamic therapy with verteporfin alone, or with the addition of 20 mg/day of selective cytokine inhibitory drug (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisoindoline 1,3-dione. The neovascular cascade is sufficiently hindered in the group receiving (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisoindoline 1,3-dione to indefinitely prolong the effects of the photodynamic therapy.
 AN 2004:392056 CAPLUS <<LOGINID::20080219>>
 DN 140:386062
 TI Methods of using and compositions comprising selective cytokine inhibitory drugs for treatment and management of macular degeneration
 IN Zeldis, Jerome B.
 PA USA
 SO U.S. Pat. Appl. Publ., 19 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

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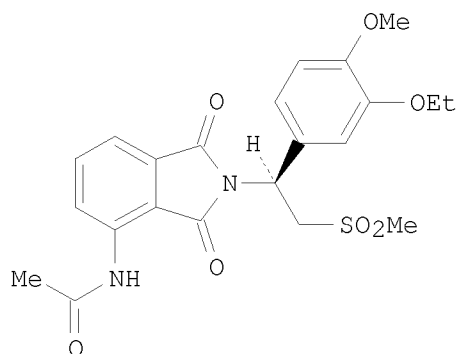
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 US 2003-699110 A 20031030
 WO 2003-US34535 W 20031031
 WO 2004-US13253 W 20040428
 OS MARPAT 140:386062

L5 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-
 acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting
 TNF- α production and PDE4 activity

GI



AB The invention discloses stereomerically pure (S)-2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione (+)-I, substantially free of its (-)-isomer, and prodrugs, metabolites, polymorphs, salts, solvates, hydrates, and clathrates thereof. Methods of using and pharmaceutical compns. comprising (+)-I for treating and/or preventing disorders ameliorated by the reduction of levels of tumor necrosis factor α (TNF- α) or the inhibition of phosphodiesterase IV (PDE4) are also disclosed. Examples include the synthesis and resolution of (+)-I, thirteen bioassays, an aqueous solubility study, and three formulations. For instance, 3-nitrophthalic acid was hydrogenated using 10% Pd/C in EtOH to give the amine (84%), which was condensed with Ac2O to afford 3-acetamidophthalic anhydride (61%). Reaction of the phthalic anhydride with 1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethylamine to give I (59%), followed by resolution with N-acetyl-L-leucine in MeOH provided (+)-I (90% recovery, 98.4% ee). The latter inhibited LPS-induced TNF- α production by human whole blood and PDE4 activity with IC50 values of 294 nM and 73.5 nM, resp. (+)-I showed >500-fold to >40,000-fold selectivity for PDE4 over PDE1, PDE2, PDE3, PDE5, and PDE6. In addition, (+)-I suppressed

LPS-induced lung neutrophilia in conscious ferrets with an ED50 of 0.8 mg/kg. Thus, (+)-I and its pharmaceutical compns. are useful for treating and/or preventing cancer, depression, and a variety of allergic, inflammatory, and autoimmune disorders (no data).

AN 2003:777583 CAPLUS <<LOGINID::20080219>>

DN 139:296870

TI Use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisindoline-1,3-dione and compositions thereof for inhibiting TNF- α production and PDE4 activity

IN Schafer, Peter H.; Muller, George W.; Man, Hon-Wah; Ge, Chuansheng

PA Celgene Corporation, USA

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

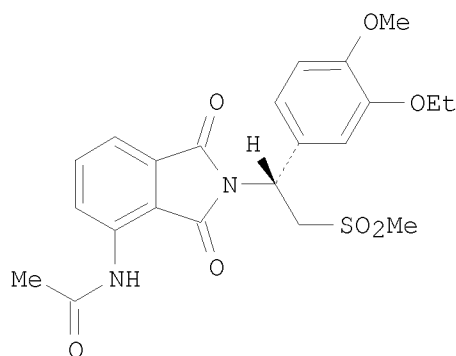
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| PI | WO 2003080049 | A1 | 20031002 | WO 2003-US8738 | 20030320 | <-- |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| | CA 2479666 | A1 | 20031002 | CA 2003-2479666 | 20030320 | <-- |
| | AU 2003224729 | A1 | 20031008 | AU 2003-224729 | 20030320 | <-- |
| | AU 2003224729 | B2 | 20080103 | | | |
| | EP 1485087 | A1 | 20041215 | EP 2003-721414 | 20030320 | <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| | CN 1652772 | A | 20050810 | CN 2003-811093 | 20030320 | <-- |
| | JP 2005525386 | T | 20050825 | JP 2003-577877 | 20030320 | <-- |
| | NZ 535798 | A | 20060428 | NZ 2003-535798 | 20030320 | <-- |
| | CN 1965823 | A | 20070523 | CN 2006-10137407 | 20030320 | <-- |
| | MX 2004PA09075 | A | 20050713 | MX 2004-PA9075 | 20040920 | <-- |
| | US 2008027123 | A1 | 20080131 | US 2007-824523 | 20070629 | <-- |
| PRAI | US 2002-366515P | P | 20020320 | <-- | | |
| | US 2003-438450P | P | 20030107 | | | |
| | US 2003-392195 | A3 | 20030319 | | | |
| | CN 2003-811093 | A3 | 20030320 | | | |
| | WO 2003-US8738 | W | 20030320 | | | |
| | US 2005-170308 | A3 | 20050628 | | | |

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Use of (-)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisindoline-1,3-dione and compositions thereof for inhibiting TNF- α production and PDE4 activity

GI



AB The invention discloses stereomerically pure (R)-2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-acetylaminoisoindoline-1,3-dione (-)-I, substantially free of its (+)-isomer, and prodrugs, metabolites, polymorphs, salts, solvates, hydrates, and clathrates thereof. Methods of using and pharmaceutical compns. comprising (-)-I for treating and/or preventing disorders ameliorated by the reduction of levels of tumor necrosis factor α (TNF- α) or the inhibition of phosphodiesterase IV (PDE4) are also disclosed. Examples include the synthesis and resolution of (-)-I, seven bioassays, an aqueous solubility study, and three formulations.

For instance, 3-nitrophthalic acid was hydrogenated using 10% Pd/C in EtOH to give the amine (84%), which was condensed with Ac2O to afford 3-acetamidophthalic anhydride (61%). Reaction of the phthalic anhydride with 1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethylamine to give I (59%), followed by resolution with N-acetyl-D-leucine in MeOH provided (-)-I (90% recovery, 98.4% ee). The latter inhibited LPS-induced TNF- α production by human whole blood and PDE4 activity with IC50 values of 371 nM and 611 nM, resp. (-)-I showed >45-fold to >39,000-fold selectivity for PDE4 over PDE1, PDE2, PDE3, PDE5, and PDE6. Thus, (-)-I and its pharmaceutical compns. are useful for treating and/or preventing cancer, depression, and a variety of allergic, inflammatory, and autoimmune disorders (no data).

AN 2003:777582 CAPLUS <<LOGINID::20080219>>

DN 139:296869

TI Use of (-)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonyl-ethyl]-4-acetylaminoisoindoline-1,3-dione and compositions thereof for inhibiting TNF- α production and PDE4 activity

IN Schafer, Peter H.; Muller, George W.; Man, Hon-Wah; Ge, Chuansheng

PA Celgene Corporation, USA

SO PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

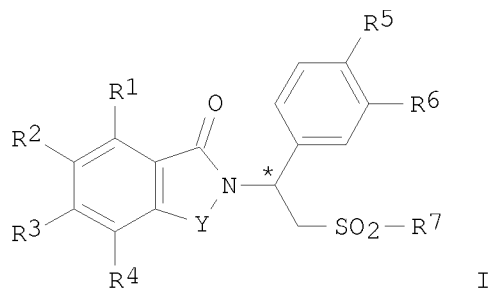
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|--------------|
| PI | WO 2003080048 | A1 | 20031002 | WO 2003-US8737 | 20030320 <-- |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | |

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003222034 A1 20031008 AU 2003-222034 20030320 <--
 PRAI US 2002-366516P P 20020320 <--
 US 2003-438448P P 20030107
 WO 2003-US8737 W 20030320

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
 TI Interactions between myeloma and endothelial cells and the effects of
 thalidomide and its analogues
 AB Modeling the situation observed in vivo, the authors examined the effects of
 thalidomide and its analogs in co-cultures of myeloma and endothelial
 cells. It was found that myeloma cells in co-culture had significantly
 lower levels of CC-10004- and CC-1088-induced apoptosis than those
 cultured alone. Interestingly, basal apoptosis was also lower in
 RPMI-8226/S co-cultured with endothelial cells compared to myeloma cell
 culture. The authors' data suggest that myeloma/endothelial cell
 interactions in co-culture have a significant protective effect on both
 basal and drug-induced levels of apoptosis in myeloma cells.
 AN 2003:649755 CAPLUS <<LOGINID::20080219>>
 DN 140:228565
 TI Interactions between myeloma and endothelial cells and the effects of
 thalidomide and its analogues
 AU Molostvov, G.; Morris, A.; Rose, P.; Basu, S.
 CS University of Warwick, Coventry, UK
 SO Free Papers - Annual Meeting of the European Haematology Association, 7th,
 Florence, Italy, June 6-9, 2002 (2002), 263-266 Publisher:
 Monduzzi Editore, Bologna, Italy.
 CODEN: 69EIOR; ISBN: 88-323-2606-X
 DT Conference
 LA English
 RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of substituted phenethylsulfones for reducing TNF α
 levels
 GI



AB The title compds. [I; the carbon atom designated "*" constitutes a center
 of chirality; Y = CO, CH2< CH2CO; R1-R4 = H, halo, alkyl, etc.; R5, R6 =
 H, alkyl, alkoxy, etc.; R7 = OH, alkyl, Ph, etc.] which reduce the levels
 of TNF α and inhibit PDE IV in a mammal (no data), were prepared and

formulated. Typical embodiments are 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-aminoisoindoline-1,3-dione and 2-[1-(3-cyclopentyloxy-4-methoxyphenyl)-2-methylsulfonylethyl]isoindoline-1,3-dione.

AN 2000:78904 CAPLUS <<LOGINID::20080219>>

DN 132:107873

TI Preparation of substituted phenethylsulfones for reducing TNF α levels

IN Muller, George W.; Man, Hon-wah

PA Celgene Corporation, USA

SO U.S., 13 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | US 6020358 | A | 20000201 | US 1998-183049 | 19981030 <-- |
| | US 6011050 | A | 20000104 | US 1999-340617 | 19990629 <-- |
| | CA 2348993 | A1 | 20000511 | CA 1999-2348993 | 19991019 <-- |
| | WO 2000025777 | A1 | 20000511 | WO 1999-US24376 | 19991019 <-- |
| | W: AU, BR, CA, IL, IS, JP, LU, NO, NZ, PT, RU, SE, SG, ZA, AM, AZ, BY, KG, KZ, MD, TJ, TM | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | EP 1126839 | A1 | 20010829 | EP 1999-971317 | 19991019 <-- |
| | EP 1126839 | B1 | 20070103 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | |
| | BR 9915201 | A | 20011030 | BR 1999-15201 | 19991019 <-- |
| | JP 2002528496 | T | 20020903 | JP 2000-579218 | 19991019 <-- |
| | AU 756308 | B2 | 20030109 | AU 2000-14472 | 19991019 <-- |
| | NZ 511253 | A | 20030228 | NZ 1999-511253 | 19991019 <-- |
| | AT 350033 | T | 20070115 | AT 1999-971317 | 19991019 <-- |
| | EP 1752148 | A2 | 20070214 | EP 2006-23050 | 19991019 <-- |
| | EP 1752148 | A3 | 20070314 | | |
| | R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | ES 2278467 | T3 | 20070801 | ES 1999-971317 | 19991019 <-- |
| | NO 2001002021 | A | 20010626 | NO 2001-2021 | 20010424 <-- |
| | NO 319790 | B1 | 20050912 | | |
| | HK 1038696 | A1 | 20070803 | HK 2002-100185 | 20020110 <-- |
| PRAI | US 1998-183049 | A3 | 19981030 | <-- | |
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| | WO 1999-US24376 | W | 19991019 | <-- | |

OS MARPAT 132:107873

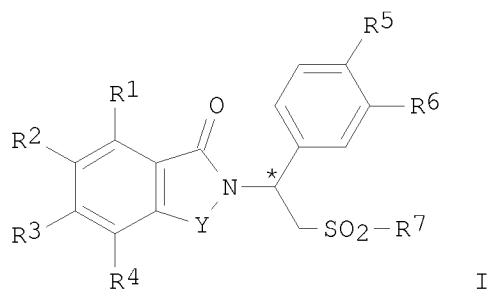
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of substituted phenethylsulfones and method of reducing TNF α levels

GI



AB The title compds. [I; the carbon atom designated * constitutes a center of chirality; Y = SO₂, CO, CH₂; R₁-R₄ = H, halo, alkyl, etc.; R₅, R₆ = H, alkyl, alkoxy, etc.; R₇ = OH, alkyl, Ph, etc.], useful in reducing the levels of TNF α and inhibiting PDE IV (no data), were prepared and formulated. Typical embodiments are 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-aminoisoindoline-1,3-dione and 2-[1-(3-cyclopentyloxy-4-methoxyphenyl)-2-methylsulfonylethyl]isoindoline-1,3-dione (preps. were given).

AN 2000:10631 CAPLUS <<LOGINID::20080219>>

DN 132:64167

TI Preparation of substituted phenethylsulfones and method of reducing TNF α levels

IN Muller, George W.; Man, Hon-Wah

PA Celgene Corporation, USA

SO U.S., 12 pp., Division of U.S. Ser. No. 183,049.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------------|------|----------|-----------------|--------------|
| PI | US 6011050 | A | 20000104 | US 1999-340617 | 19990629 <-- |
| | US 6020358 | A | 20000201 | US 1998-183049 | 19981030 <-- |
| PRAI | US 1998-183049 | A3 | 19981030 | <-- | |
| OS | MARPAT 132:64167 | | | | |

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:01:56 ON 19 FEB 2008)

FILE 'REGISTRY' ENTERED AT 08:02:03 ON 19 FEB 2008

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 3 S L1 FAM FULL

FILE 'CAPLUS' ENTERED AT 08:02:39 ON 19 FEB 2008

L4 19 S L3

L5 10 S L4 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> log hold

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

35.94

106.26

| | | |
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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -8.00 | -8.00 |

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:03:19 ON 19 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEXO1623

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 08:39:00 ON 19 FEB 2008
FILE 'CAPLUS' ENTERED AT 08:39:00 ON 19 FEB 2008
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 35.94 | 106.26 |

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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -8.00 | -8.00 |

```
=> s (complex regional pain) or (reflex sympathetic dysrophy)
    1391653 COMPLEX
      71428 REGIONAL
      56916 PAIN
        172 COMPLEX REGIONAL PAIN
          (COMPLEX(W)REGIONAL(W)PAIN)
        26038 REFLEX
        40928 SYMPATHETIC
          0 DYSROPHY
          0 REFLEX SYMPATHETIC DYSROPHY
            (REFLEX(W)SYMPATHETIC(W)DYSROPHY)
L6      172 (COMPLEX REGIONAL PAIN) OR (REFLEX SYMPATHETIC DYSROPHY)
```

```
=> s 15 and 16
L7      0 L5 AND L6
```

```
=> s 14 and 16
L8      0 L4 AND L6
```

```
=> fioe stnguide
FIOE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

```
=> file stnguide
```

| | | |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
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| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -8.00 | -8.00 |

FILE 'STNGUIDE' ENTERED AT 08:40:07 ON 19 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Feb 15, 2008 (20080215/UP).

| | | |
|--|------------|---------|
| => file hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.06 | 120.00 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -8.00 |

FILE 'HCAPLUS' ENTERED AT 08:40:43 ON 19 FEB 2008
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FILE COVERS 1907 - 19 Feb 2008 VOL 148 ISS 8
 FILE LAST UPDATED: 18 Feb 2008 (20080218/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (TNF-alpha) or (tumor necrosis factor)

```

      74205 TNF
    1744875 ALPHA
      56281 TNF-ALPHA
            (TNF(W)ALPHA)
      440722 TUMOR
      136064 NECROSIS
     1101543 FACTOR
      73322 TUMOR NECROSIS FACTOR
            (TUMOR(W)NECROSIS(W)FACTOR)
L9      92620 (TNF-ALPHA) OR (TUMOR NECROSIS FACTOR)

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=> s 15 and 19

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      19 L3
    22928631 PY<2003
    4476249 AY<2003

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3951450 PRY<2003
L10 5 L5 AND L9

=> file stnguide

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 2.69 | 122.69 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -8.00 |

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

=> file hcaplus

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|--|------------------|---------------|
| FULL ESTIMATED COST | 0.12 | 122.81 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -8.00 |

FILE 'HCAPLUS' ENTERED AT 08:41:53 ON 19 FEB 2008
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FILE COVERS 1907 - 19 Feb 2008 VOL 148 ISS 8
FILE LAST UPDATED: 18 Feb 2008 (20080218/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s (complex regional pain) or (reflex sympathetic dystrophy)

1391653 COMPLEX
71428 REGIONAL
56916 PAIN
172 COMPLEX REGIONAL PAIN
(COMPLEX(W)REGIONAL(W)PAIN)
26038 REFLEX

40928 SYMPATHETIC
13836 DYSTROPHY
202 REFLEX SYMPATHETIC DYSTROPHY
(REFLEX(W)SYMPATHETIC(W)DYSTROPHY)
L11 347 (COMPLEX REGIONAL PAIN) OR (REFLEX SYMPATHETIC DYSTROPHY)

=> s 19 and l11

L12 26 L9 AND L11

=> s l12 and (PY<2003 or AY<2003 or PRY<2003)

22928631 PY<2003
4476249 AY<2003
3951450 PRY<2003
L13 9 L12 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file stnguide

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 2.69 | 125.50 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -8.00 |

FILE 'STNGUIDE' ENTERED AT 08:41:58 ON 19 FEB 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

=> d l13 1-9 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L13 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Use of TNF- α inhibitors for treating nerve root
injury and other nerve disorders
AB The invention discloses a method for treating nerve disorders in a mammal
or a vertebrate by administering a TNF- α
inhibitor. The invention also discloses the use of a TNF- α
inhibitor in the preparation of pharmaceutical compns. for the
treatment of nerve root injury and other nerve disorders.
AN 2008:97252 HCAPLUS <<LOGINID::20080219>>
TI Use of TNF- α inhibitors for treating nerve root
injury and other nerve disorders
IN Olmarker, Kjell; Rydevik, Bjorn
PA Swed.
SO U.S. Pat. Appl. Publ., 29pp., Cont.-in-part of U.S. Ser. No. 521,093.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-----------------|--------------|
| ----- | ---- | ----- | ----- | ----- |
| PI US 2008019964 | A1 | 20080124 | US 2007-648957 | 20070103 <-- |

| | | | | |
|---|----|----------|----------------|--------------|
| SE 9803710 | A | 20000326 | SE 1998-3710 | 19981029 <-- |
| WO 2000018409 | A1 | 20000406 | WO 1999-SE1671 | 19990923 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, | | | | |
| CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, | | | | |
| IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, | | | | |
| MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, | | | | |
| SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, | | | | |
| DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, | | | | |
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| US 6649589 | B1 | 20031118 | US 2001-743852 | 20010117 <-- |
| US 2001055594 | A1 | 20011227 | US 2001-826893 | 20010406 <-- |
| US 2003039651 | A1 | 20030227 | US 2002-225237 | 20020822 <-- |
| US 7115557 | B2 | 20061003 | | |
| US 2007104711 | A1 | 20070510 | US 2006-521093 | 20060914 <-- |
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| SE 1998-3710 | A | 19981029 | <-- | |
| WO 1999-SE1671 | W | 19990923 | <-- | |
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| US 2002-225237 | A2 | 20020822 | <-- | |
| US 2006-521093 | A2 | 20060914 | | |

L13 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Method of biochemical treatment of persistent pain by inhibiting biochemical mediators of inflammation

AB The invention discloses a method for the biochem. treatment of persistent pain disorders by inhibiting the biochem. mediators of inflammation in a subject, comprising administering to the subject any one of several combinations of components that are inhibitors of biochem. mediators of inflammation. The process for biochem. treatment of persistent pain disorders is based on Sota Omoigui's Law, which states: 'The origin of all pain is inflammation and the inflammatory response'. Sota Omoigui's Law of Pain unifies all pain syndromes as sharing a common origin of inflammation and the inflammatory response. The various biochem. mediators of inflammation are present in differing amts. in all pain syndromes and are responsible for the pain experience. Classification and treatment of pain syndromes should depend on the complex inflammatory profile. A variety of mediators are generated by tissue injury and inflammation. These include substances produced by damaged tissue, substances of vascular origin as well as substances released by nerve fibers themselves, sympathetic fibers and various immune cells. Biochem. mediators of inflammation that are targeted for inhibition include but are not limited to: prostaglandin, nitric oxide, tumor necrosis factor α , interleukin 1α , interleukin 1β , interleukin 4, Interleukin 6, and interleukin 8, histamine and serotonin, substance P, matrix metalloproteinase, calcitonin gene-related peptide, vasoactive intestinal peptide, as well as the potent inflammatory mediator peptide proteins neurokinin A, bradykinin, kallidin and T-kinin.

AN 2005:611671 HCAPLUS <<LOGINID::20080219>>

DN 143:126805

TI Method of biochemical treatment of persistent pain by inhibiting biochemical mediators of inflammation

IN Omoigui, Osemwota Sota

PA USA

SO U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 224,743.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 6

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|--------------|
| PI | US 2005152905 | A1 | 20050714 | US 2005-58371 | 20050216 <-- |
| | US 2004038874 | A1 | 20040226 | US 2002-224743 | 20020822 <-- |
| | US 2006275294 | A1 | 20061207 | US 2006-279239 | 20060410 <-- |
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| | US 2005-268609 | A2 | 20051108 | | |

L13 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Methods of using and compositions comprising selective cytokine inhibitory drug for treatment, modification and management of pain

AB Methods of treating, preventing, modifying and managing various types of pain are disclosed. Specific methods comprise the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical comps., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

AN 2005:426388 HCAPLUS <<LOGINID::20080219>>

DN 142:457121

TI Methods of using and compositions comprising selective cytokine inhibitory drug for treatment, modification and management of pain

IN Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.

PA Celgene Corporation, USA

SO PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DT Patent

LA English

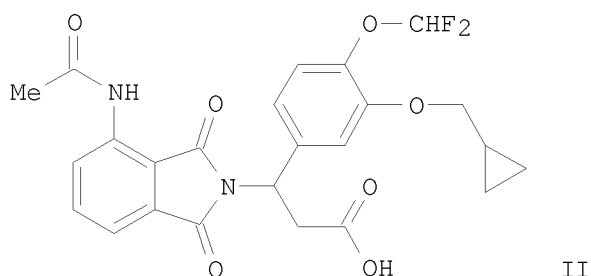
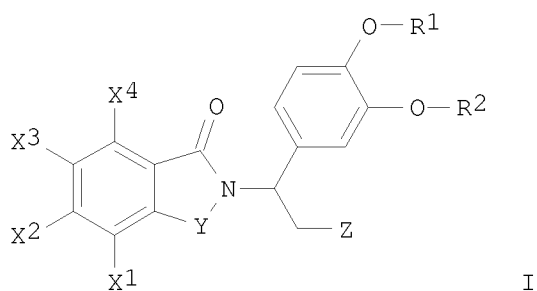
FAN.CNT 6

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|------------------|--------------|
| PI | WO 2005043971 | A2 | 20050519 | WO 2004-US12722 | 20040423 |
| | WO 2005043971 | A3 | 20050714 | | |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: | | | | |
| | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2005203142 | A1 | 20050915 | US 2003-693794 | 20031023 <-- |
| | AU 2004286819 | A1 | 20050519 | AU 2004-286819 | 20040423 |
| | CA 2543132 | A1 | 20050519 | CA 2004-2543132 | 20040423 |
| | EP 1679967 | A2 | 20060719 | EP 2004-750613 | 20040423 |
| | R: | | | | |
| | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | BR 2004015649 | A | 20061219 | BR 2004-15649 | 20040423 |
| | CN 1897816 | A | 20070117 | CN 2004-80038252 | 20040423 |
| | JP 2007524656 | T | 20070830 | JP 2006-536543 | 20040423 |
| | MX 2006PA04381 | A | 20060706 | MX 2006-PA4381 | 20060420 |
| | US 2007161696 | A1 | 20070712 | US 2007-576139 | 20070102 |
| PRAI | US 2003-693794 | A | 20031023 | | |
| | US 2002-421003P | P | 20021024 | <-- | |
| | US 2003-693722 | A | 20031023 | | |

L13 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as
PDE4, TNF- α , and/or MMP inhibitors

GI



AB Title compds. I [wherein X1-X4 = independently H, halo, NO₂, NH₂, CF₃, alkyl, cycloalkyl(alkyl), NR₇R₈-(alkyl), R₈CONH-(alkyl), NR₇R₈CONH-(alkyl), R₈OCONH-(alkyl), R₈O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH₂, CH₂CO, COCH₂, SO₂; Z = H, COR₃, alkylsulfonyl(alkyl), alkyl, CH₂OH, alkoxymethyl, CN; R₁ and R₂ = independently CHF₂, alkyl, cycloalkyl(alkyl); at least one of R₁ and R₂ = CHF₂; R₃ = NR₄R₅, alkyl, OH, alkoxy, (un)substituted Ph, PhCH₂; R₄ and R₅ = independently H, alkyl, OH, OCOR₆; R₆ = alkyl(amino), Ph, PhCH₂, aryl; R₇ and R₈ = independently H, alkyl, cycloalkyl(alkyl), NR₇R₈-alkyl, R₈O-alkyl, Ph, PhCH₂, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepared For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of K₂CO₃ in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addition of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindolone II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases associated with phosphodiesterase 4

(PDE4) inhibition, abnormal tumor necrosis factor α (TNF- α) levels, and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

AN 2004:589381 HCAPLUS <<LOGINID::20080219>>

DN 141:140314

TI Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as PDE4, TNF- α , and/or MMP inhibitors

IN Muller, George W.; Man, Hon-Wah; Zhang, Weihong

PA Celgene Corporation, USA

SO PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|------------------|--------------|
| PI | WO 2004060313 | A2 | 20040722 | WO 2003-US41568 | 20031229 <-- |
| | WO 2004060313 | A3 | 20050915 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2511843 | A1 | 20040722 | CA 2003-2511843 | 20031229 <-- |
| | AU 2003303511 | A1 | 20040729 | AU 2003-303511 | 20031229 <-- |
| | US 2004204448 | A1 | 20041014 | US 2003-748085 | 20031229 <-- |
| | US 7173058 | B2 | 20070206 | | |
| | EP 1587474 | A2 | 20051026 | EP 2003-808605 | 20031229 <-- |
| | EP 1587474 | A3 | 20051102 | | |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| | BR 2003017885 | A | 20051206 | BR 2003-17885 | 20031229 <-- |
| | JP 2006515310 | T | 20060525 | JP 2004-565816 | 20031229 <-- |
| | CN 1802353 | A | 20060712 | CN 2003-80109907 | 20031229 <-- |
| | MX 2005PA06998 | A | 20050818 | MX 2005-PA6998 | 20050627 <-- |
| | US 2007072902 | A1 | 20070329 | US 2006-601355 | 20061116 <-- |
| PRAI | US 2002-436975P | P | 20021230 | <-- | |
| | US 2003-748085 | A3 | 20031229 | | |
| | WO 2003-US41568 | W | 20031229 | | |
| OS | MARPAT 141:140314 | | | | |

L13 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Methods for the treatment of pain and traumatic injury using benzamides and compositions containing the same

AB Methods are disclosed for treating and preventing pain such as neuropathic pain, and traumatic injuries such as traumatic brain injury and acute spinal cord injury, which comprise administering effective amts. of a benzamide compound Pharmaceutical compns., dosage forms and methods of administration are set forth.

AN 2004:589365 HCAPLUS <<LOGINID::20080219>>

DN 141:117179

TI Methods for the treatment of pain and traumatic injury using benzamides and compositions containing the same

IN Goodman, Corey R.; Serafini, Tito
 PA Renovis, Inc., USA
 SO PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|--------------|
| PI | WO 2004060286 | A2 | 20040722 | WO 2003-US39895 | 20031216 <-- |
| | WO 2004060286 | A3 | 20041104 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2004167226 | A1 | 20040826 | US 2003-736460 | 20031215 <-- |
| | CA 2510042 | A1 | 20040722 | CA 2003-2510042 | 20031216 <-- |
| | AU 2003300939 | A1 | 20040729 | AU 2003-300939 | 20031216 <-- |
| | EP 1581202 | A2 | 20051005 | EP 2003-814819 | 20031216 <-- |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| | JP 2006514056 | T | 20060427 | JP 2004-565509 | 20031216 <-- |
| | MX 2005PA06573 | A | 20060222 | MX 2005-PA6573 | 20050616 <-- |
| PRAI | US 2002-434022P | P | 20021216 | <-- | |
| | US 2003-736460 | A | 20031215 | | |
| | WO 2003-US39895 | W | 20031216 | | |

L13 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Method of treatment of persistent pain by inhibiting mediators of inflammation

AB This invention relates to a method for treating persistent pain disorders by inhibiting the biochem. mediators of inflammation in a subject comprising administering to said subject a therapeutically effective dosage of said inhibitor. Said process for treating persistent pain disorders is based on Sota Omoigui's Law, which states: The origin of all pain is inflammation and the inflammatory response. Biochem. mediators of inflammation that are targeted for inhibition include but are not limited to: prostaglandin, nitric oxide, tumor necrosis factor alpha, interleukin 1-alpha, interleukin 1-beta, interleukin-4, Interleukin-6 and interleukin-8, histamine and serotonin, substance P, Matrix Metallo-Proteinase, calcitonin gene-related peptide, vasoactive intestinal peptide as well as the potent inflammatory mediator peptide proteins neurokinin A, bradykinin, kallidin and T-kinin.

AN 2004:162447 HCAPLUS <<LOGINID::20080219>>

DN 140:193061

TI Method of treatment of persistent pain by inhibiting mediators of inflammation

IN Omoigui, Osemwota

PA USA

SO U.S. Pat. Appl. Publ., 14 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 6

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

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|------|----------------|----|----------|----------------|--------------|
| PI | US 2004038874 | A1 | 20040226 | US 2002-224743 | 20020822 <-- |
| | US 2005152905 | A1 | 20050714 | US 2005-58371 | 20050216 <-- |
| | US 2006275294 | A1 | 20061207 | US 2006-279239 | 20060410 <-- |
| PRAI | US 2002-224743 | A2 | 20020822 | <-- | |
| | US 2004-961037 | A2 | 20041012 | | |
| | US 2005-58371 | A2 | 20050216 | | |
| | US 2005-122030 | A2 | 20050505 | | |
| | US 2005-268609 | A2 | 20051108 | | |

L13 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Cytokine antagonists inhibiting tumor necrosis factor or interleukin-1 for treating neurological and neuropsychiatric disorders

AB Methods for treating neurol. or neuropsychiatric diseases or disorders in humans by administering to the human a therapeutically ED of specific biologics are presented. The biologics of consideration include antagonists of tumor necrosis factor or of interleukin-1. The administration of these biologics is performed by specific methods, most, but not all of which fall into the category of anatomically localized administration designed for perispinal use. Anatomically localized administration involving perispinal use includes, but is not limited to the s.c., i.m., interspinous, epidural, peridural, parenteral or intrathecal routes. Addnl., intranasal administration is discussed as a method to provide therapeutic benefit. The clin. conditions of consideration include, but are not limited to the following: diseases of the brain, including neurodegenerative diseases such as Alzheimer's Disease and Parkinson's Disease; migraine headache; spinal radiculopathy associated with intervertebral disk herniation, post-herpetic neuralgia, reflex sympathetic dystrophy, neuropathic pain, vertebral disk disease, low back pain, amyotrophic lateral sclerosis, chronic fatigue syndrome; and neuropsychiatric diseases, including bipolar affective disorder, anorexia nervosa, nicotine withdrawal, narcotic addiction, alc. withdrawal, postpartum depression, and schizoaffective illness.

AN 2003:203189 HCAPLUS <<LOGINID::20080219>>

DN 138:215342

TI Cytokine antagonists inhibiting tumor necrosis factor or interleukin-1 for treating neurological and neuropsychiatric disorders

IN Tobinick, Edward Lewis

PA USA

SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 236,097.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 12

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|--------------|
| | ----- | ---- | ----- | ----- | ----- |
| PI | US 2003049256 | A1 | 20030313 | US 2002-269745 | 20021009 <-- |
| | US 6982089 | B2 | 20060103 | | |
| | US 6015557 | A | 20000118 | US 1999-275070 | 19990323 <-- |
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W: AU, CA, JP, NO, NZ, SE

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

| | | | | | | |
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RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Evidence for local inflammation in complex regional
pain syndrome type 1

AB BACKGROUND: The pathophysiol. of complex regional
pain syndrome type 1 (CRPS 1) is still a matter of debate.
Peripheral afferent, efferent and central mechanisms are supposed. Based
on clin. signs and symptoms (e.g. edema, local temperature changes and chronic
pain) local inflammation is suspected. Aim: To determine the involvement of
neuropeptides, cytokines and eicosanoids as locally formed mediators of
inflammation. Methods: In this study, nine patients with proven CRPS 1
were included. Disease activity and impairment was determined by means of a
Visual Analog Scale, the McGill Pain Questionnaire, the difference in volume
and temperature between involved and uninvolved extremities, and the reduction

in

active range of motion of the involved extremity. Venous blood was
sampled from and suction blisters made on the involved and uninvolved
extremities for measurement of cytokines interleukin (IL)-6, IL-1 β
and tumor necrosis factor- α (TNF- α), the neuropeptides NPY and CRGP, and
prostaglandin E2. Results: The patients included in this study did have a
moderate to serious disease activity and impairment. In plasma, no
changes of mediators of inflammation were observed. In blister fluid,
however, significantly higher levels of IL-6 and TNF- α . in the involved extremity were observed in comparison with the
uninvolved extremity. Conclusions: This is the first time that
involvement of mediators of inflammation in CRPS 1 has been so clearly and
directly demonstrated. This observation opens new approaches for the
successful use and development of immunosuppressives in CRPS 1.

AN 2002:305303 HCAPLUS <<LOGINID::20080219>>

DN 137:167971

TI Evidence for local inflammation in complex regional
pain syndrome type 1

AU Huygen, Frank J. P. M.; De Bruijn, Anke G. J.; De Bruin, Martha T.;
Groeneweg, J. George; Klein, Jan; Zijlstra, Freek J.

CS Pain Treatment Centre, Erasmus Medical Centre, Rotterdam, 3000 CA, Neth.

SO Mediators of Inflammation (2002), 11(1), 47-51

CODEN: MNFLEF; ISSN: 0962-9351

PB Taylor & Francis Ltd.

DT Journal

LA English

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Increased production of nitric oxide stimulated by interferon- γ from
peripheral blood monocytes in patients with complex
regional pain syndrome
AB This study examines immediate nitric oxide (NO) release from monocytes
following interleukin-1 β (IL-1 β), interferon- γ
(IFN- γ), and tumor necrosis factor
- α (TNF- α) challenge in patients with
complex regional pain syndrome (CRPS). Study
patients exhibited the following: (1), mech. allodynia; (2), evidence of
either vasomotor or sudomotor disturbance; and (3), concordant painful
allodynia documented with quant. sensory testing that was temporarily
abolished with sympathetic block. Ten subjects (CRPS, N=5; control, N=5)
were enrolled. Peripheral blood monocytes were challenged with 100 μ L
of IL-1 β (1 ng), IFN- γ (1 ng), TNF- α
(0.01 ng), and normal saline (NS) and the resultant immediate NO release
measured. Subjects with CRPS exhibited a statistically significant
increase in NO release in response to IFN- γ compared with controls.
The NO responses to IFN- γ in excess of NS and as the ratio
IFN- γ /NS were also significantly increased.
AN 2002:212993 HCAPLUS <<LOGINID::20080219>>
DN 136:368210
TI Increased production of nitric oxide stimulated by interferon- γ from
peripheral blood monocytes in patients with complex
regional pain syndrome
AU Hartrick, Craig T.
CS Department of Anesthesiology and Perioperative Medicine, William Beaumont
Hospital, Royal Oak, MI, 48073, USA
SO Neuroscience Letters (2002), 323(1), 75-77
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT